7. Filip, Z., Haider, K., Beutelspacher, H. & Martin, J. P. *Geoderma* **11,** 37–52 (1974).
8. Yakubu, N. A. & Dudeney, A. W. L. in *Immobilisation of Ions by Bio-sorption* (eds Eccles, H. & Hunt, S.) 183–200 (Ellis Horwood, Chichester, 1986).
9. Ramelow, G. J. *et al. Int. J. Environ. Anal. Chem.* **53,** 213–232 (1993).
10. Huneck, S. & Yoshimura, S. *Identification of Lichen Substances* (Springer, Berlin, 1997).

Electric current stimulates laughter

Speech and laughter are uniquely human. Although there is considerable information on the neuronal representation of speech, little is known about brain mechanisms of laughter. Here we report that electrical stimulation in the anterior part of the human supplementary motor area (SMA) can elicit laughter. This area is also involved in the initiation of speech and has been shown to have increased activity in people who stutter[1].

Electrical stimulation was applied at 85 discrete sites on the cortical surface of the left frontal lobe of a 16-year-old girl (A.K.) undergoing monitoring by intracranial subdural electrodes to locate the focus of chronic intractable seizures. The patient's seizures were never accompanied by laughter. During stimulation A.K. performed a variety of tasks including naming of objects, reading a paragraph of text, counting, rapid alternating supination and pronation of the forearms, finger-to-thumb apposition, and alternating flexion and dorsiflexion of the feet.

A small area measuring about 2 cm × 2 cm was identified on the left superior frontal gyrus where stimulation consistently produced laughter (Fig. 1, red circles). The laughter was accompanied by a sensation of merriment or mirth. Although it was evoked by stimulation on several trials, a different explanation for it was offered by the patient each time, attributing the laughter to whatever external stimulus was present. Thus, laughter was attributed to the particular object seen during naming ("the horse is funny"), to the particular content of a paragraph during reading, or to persons present in the room while the patient performed a finger apposition task ("you guys are just so funny… standing around").

The duration and intensity of laughter increased with the level of stimulation current. At low currents only a smile was present, while at higher currents a robust contagious laughter was induced. It was also accompanied by the cessation of all activities involving speech or hand movements. At neighbouring sites, speech arrest was provoked without the evocation of laughter (Fig. 1, yellow circles), and at medially adjacent sites stimulation arrested all manual and speech activities (Fig. 1, blue circles). These sites were anterior to the area where electrical stimulation evoked complex responses involving lower and upper extremities typical of the supplementary motor area (Fig. 1, black circles)[2,3]. The area encompassing sites of laughter, speech arrest and manual activity extended to the dorsal convexity of the hemisphere, in agreement with current notions about the lateral border of the SMA[4].

Pathological laughter has been described in several clinical conditions, including pseudobulbar palsy and gelastic seizures associated with lesions in the hypothalamus or temporal lobe[5,6]. However, laughter in these conditions is rarely associated with the appropriate emotional experience, and often the condition of the patient (for example, a seizure) precludes reporting of the emotional experience. There are a very few reports of laughter evoked by electrical stimulation at cortical sites including the anterior cingulate and orbitofrontal cortex[7] and the basal temporal lobe[5]. Arroyo *et al.* postulated dissociation of the motor program of laughter and the experience of merriment, localizing the former in the anterior cingulate and the latter in the temporal lobe[5]; however, our data show that laughter and mirth can be evoked by stimulation of the frontal cortex in the anterior part of the SMA, an area associated with the execution of motor programs.

Figure 1 Magnetic resonance imaging three-dimensional surface reconstruction of left hemisphere of patient A.K., depicting sites where electrical stimulation evoked behavioural responses. Constant current electrical stimulation (1–12 mA, 0.3 ms duration, biphasic rectangular pulses), below the threshold of after-discharge, was applied at 50 Hz in a bipolar fashion for a duration of 5 s through adjacent contacts 1 cm apart on a subdural grid and strip electrodes implanted over the cortical surface of the left frontal lobe. No stimulation was performed at the right frontal lobe. Electrodes were implanted to identify the seizure focus, and electrical stimulation mapping was performed to plan the surgical resection of the focus. Informed consent was obtained in accordance with protocol approved by an internal review board. Key to colours: red, laughter; yellow, disruption or arrest of speech; blue, disruption or arrest of speech, naming and manual activity; black, motor movements involving the lower and upper extremities; green, tingling sensations in the right lower extremity. Reversal of the N20 potentials evoked by right posterior tibial nerve stimulation confirmed the location of the central sulcus at the anterior green circle.

The observation that A.K. was able each time to invoke a stimulus context that 'explained' the laughter suggests a close link between the motor, affective and cognitive components of laughter. It is likely that these varied components are represented in a large neuronal network capable of parallel distributed processing, where the entire network is activated as a whole by the stimulation of any of its constituent units[8]. Our observations also suggest that smiling and laughter might involve similar mechanisms and are closely related phenomena on a single continuum.

Although it could be argued that the neural representation of laughter observed in our epilepsy patient might not reflect the substrate for laughter in the normal brain, it should be emphasized that laughter was not a part of A.K.'s seizures. Furthermore, the region of seizure onset was medial to the area of evoked laughter, and stimulation in this region did not produce laughter responses. The human SMA has somatotopic organization, with the hands represented anterior to the arms and legs, and face and speech represented most anteriorly[3]. Our results suggest that speech and laughter are closely represented in the rostral part of the SMA, just anterior to the representation of manual activity.

We propose that the anterior part of the SMA is part of a further development in humans to accommodate the specialized functions of speech, manual dexterity and laughter. This area might correspond to the pre-supplementary motor area, a region situated anterior to the SMA proper, recently described in non-human primates, and thought to be involved in high-level motor programming[9,10].

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1. Fox, P. T. *et al. Nature* **382,** 158–161 (1996).
2. Mitz, A. R. & Wise, S. P. *J. Neurosci.* **7,** 1010–1021 (1987).
3. Fried, I. *et al. J. Neurosci.* **11,** 3656–3666 (1991).
4. Wise, S. P. *et al. Adv. Neurol.* **70,** 489–495 (1996).
5. Arroyo, S. *et al. Brain* **116,** 757–780 (1993).
6. Martin, J. P. *Brain* **73,** 453–464 (1950).
7. Sem-Jacobsen, C. W. in *Depth-electrographic Stimulation of the Human Brain and Behavior* (ed. Gantt, W. H.) 127–138 (Charles C. Thomas, Springfield, Illinois, 1968).
8. Rumelhart, D. E., & McClelland, J. L. *Parallel Distributed Processing: Explorations in the Microstructure of Cognition* vol. 1 (MIT Press, Cambridge, Massachusetts, 1978).
9. Tanji, J. *Curr. Opin. Neurobiol.* **6,** 782–787 (1996).
10. Picard, N. & Strick, P. *Cerebral Cortex* **6,** 342–353 (1996).